



Europäisches Patentamt
European Patent Office
Office européen des brevets



Publication number: **0 526 606 B1**

(12)

EUROPEAN PATENT SPECIFICATION

- (43) Date of publication of patent specification: **16.08.95** (51) Int. Cl.⁸: **A61K 9/28, B05B 5/08, B05D 1/06**
- (21) Application number: **92905114.2**
- (22) Date of filing: **21.02.92**
- (86) International application number:
PCT/GB92/00323
- (87) International publication number:
WO 92/14451 (03.09.92 92/23)

(54) **IMPROVEMENTS IN OR RELATING TO ELECTROSTATIC COATING OF SUBSTRATES OF MEDICINAL PRODUCTS.**

- (30) Priority: **22.02.91 GB 9103711**
- (43) Date of publication of application:
10.02.93 Bulletin 93/06
- (43) Publication of the grant of the patent:
16.08.95 Bulletin 95/33
- (54) Designated Contracting States:
AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE
- (56) References cited:
- | | |
|------------------------|------------------------|
| EP-A- 0 085 149 | EP-A- 0 381 044 |
| EP-A- 0 405 884 | BE-A- 522 840 |
| BE-A- 649 491 | DE-A- 2 636 152 |
| GB-A- 1 449 993 | US-A- 4 495 217 |
| US-A- 4 774 102 | |

- (73) Proprietor: **HOECHST UK LIMITED**
Hoechst House
Sallsbury Road
Hounslow
Middlesex TW4 6JH (GB)
- (72) Inventor: **STANIFORTH, John, Nicholas**
High Trees
170 Bloomfield Road
Bath
Avon BA2 2AT (GB)
Inventor: **GROSVENOR, Martin, Paul**
23 Stirlingale Avenue
Bath
Avon BA2 2NQ (GB)
- (74) Representative: **Bardo, Julian Eason et al**
Abel & Imray
Northumberland House
303-306 High Holborn
London, WC1V 7LH (GB)

Note: Within nine months from the publication of the mention of the grant of the European patent, any person may give notice to the European Patent Office of opposition to the European patent granted. Notice of opposition shall be filed in a written reasoned statement. It shall not be deemed to have been filed until the opposition fee has been paid (Art. 99(1) European patent convention).

Description

The present invention relates to a method and apparatus for electrostatic coating of pharmaceutical tablet cores with a dry powder.

Proposals for electrostatic coating of tablets have been made for at least the last thirty years or so. For example, GB-1075404 (published in 1967 and corresponding to BE 649491A) proposes an apparatus for coating tablets in which an atomiser is used to spray finely divided particles of a coating solution onto tablets in a high potential electrostatic field. A hopper supplies tablets to a first stage conveyor and a liquid is sprayed onto one face of each tablet core as the tablet cores are conveyed below a first stage sprayer having an associated high voltage grid, and the coating is dried using, for example, a first stage infra-red heater. The half coated tablets are reversed in a rotating tablet-inverting drum and are then conveyed on a second stage conveyor below a second stage sprayer having an associated high voltage grid with the other side of the tablets uppermost, and then that coating is dried again using a second stage infrared heater.

Various paper proposals (EP-A-0 148 772 and WO-A-8 603 993) for electrostatically coating tablet cores with a liquid or a dry powder have been made but as yet at least in the case of pharmaceutical tablets there is no recognized electrostatic coating method or apparatus that has proved sufficiently successful to be applied commercially on a reasonable scale. While there are rotary tablet presses capable of producing pharmaceutical tablet cores continuously at a rate of for example 5,000 tablets per minute, the subsequent coating of the tablet cores is most commonly carried out as a batch process by applying a liquid coating in a revolving drum.

In order to provide a commercially viable apparatus or method for coating tablet cores various problems must be overcome. It is in many ways easier to apply a liquid rather than a dry powder as the coating material and therefore, although both options have been considered in research, workers have favoured the use of liquids. If a dry powder is applied then it is harder to obtain adhesion of the coating to the core, which is not itself likely to be sufficiently electrically conducting, even when the powder is electrostatically charged. In order to provide a lasting bond between the core and the powder, the powder must be transformed into a film, for example by melting, but in the case of a tablet core, which in many cases will include organic materials, this must not be damaged. Furthermore an even coating is required and it is very difficult to obtain an even coating of powder on an electrically insulating tablet core, even when the powder is electrostatically charged.

When liquid coating is used, the coating must be dried. Theoretically such drying could in some circumstances be carried out at room temperature but in commercial practice it is important, for example because of the rate at which the process must be carried out, to heat the tablets and that is expensive because of the large input of energy required to vapourize the solvent used in the liquid coating. Another disadvantage of liquid coating is that it cannot be used for coating materials that are not soluble or suitably dispersible in a usable liquid, preferably water.

The electrostatic powder coating of parts is known in the prior art. For example, US 4 495 217 describes a method for the electrostatic coating of items such as busbars, wall panels, dishwasher baskets, thumbtacks, bradclips and zipper pulls using a powder coating material. The items to be coated are placed on a heat conductive conveyor belt, and the powder is sprayed onto the exposed surfaces of the parts using an electrostatic spray gun. The parts are heated using a radiant heater such that the powder on the surfaces of the parts is fused. By using the apparatus described, the need to hang the parts to be coated on J-hooks is eliminated.

US 4 774 102 describes a method for the electrostatic powder spray coating of articles, substrates and parts having electrically conductive surfaces. The method enables the use of high charging voltages for the spray gun in the spray coating of preheated substrates, without the occurrence of "cobwebbing". Corona charging may be used to charge the powder coating material. Suitable coating materials for the described method include high molecular weight thermoplastic resins and low molecular weight thermosetting resins.

It is an object of the invention to provide an improved method and apparatus for coating cores of pharmaceutical tablets.

According to the invention there is provided a method of coating cores of pharmaceutical tablets with a coating material, the method including the following steps:

- feeding the cores onto a conveying means;
- supplying the coating material to a region through which the cores are to be conveyed on the conveying means;
- conveying the cores on the conveying means through the region with the cores maintained at a different electric potential from the coating material, whereby the coating material is attracted to the exposed surfaces of the cores to form coatings thereon, characterised in that the coating material is a dry powder and that after the dry powder is attracted to the exposed surfaces of the cores to form coatings thereon the dry powder is melted to convert the powder into fused film coatings se-

cured to the cores.

By placing the cores on a conveying means during the charging process, it is found that a satisfactory spread of powder over the core can be obtained. It is also found that some unevenness of distribution is not necessarily serious, even if it is important for the final tablet to have a coating of substantially constant thickness, because further levelling can take place when the powder is converted into a fused film. Thus the present invention enables a desired thickness of coating to be applied uniformly over a surface of a tablet core. The thickness of the coating will typically be greater than 10 μm . Although the present invention as defined above still involves the input of energy to convert the powder into a fused film, the amount of energy required can be substantially less than that involved in the case where a liquid coating comprising a coating substance dissolved in a suitable solvent is applied and the solvent has to be vapourised after application of the coating. The method also removes the necessity for solvent handling and disposal and for batch processing.

While reference is made throughout the specification to "tablets" and the invention is of particular application to pharmaceutical tablets of conventional shape, it should be understood that the term is to be interpreted in a broad sense as covering also, for example, pellets, capsules or spherules.

While the method of the invention will generally be applied to the coating of tablet cores which have not received any coating since being formed in a press, it may be used to apply a coating on top of an already coated or partly coated tablet core.

The method of the present invention may be carried out as a continuous process. In practice there are considerable advantages in being able to operate the coating process continuously rather than as a batch process.

While there are certain applications, which will be referred to later, where it will be desired to coat the tablet core on one side only or with at least one discontinuity in the coating, it will generally be desirable to coat all of the exterior of the tablet core. Accordingly the method preferably comprises the following further subsequent steps:

feeding the tablet core onto a conveying means with the fused film coatings of the cores in contact with the conveying means and with that surface of the core that was in contact with the conveying means during the above-mentioned conveying step exposed;

supplying the dry powder with which the cores are to be coated to a region through which the conveying means passes;

conveying the cores on the conveying means through the region with the conveying means

and/or the cores maintained at a different electric potential from the dry powder whereby the dry powder is attracted to the exposed surfaces of the cores, and

melting the dry powder coatings to convert the newly applied powder into fused film coatings secured to the cores.

For practical convenience the conveying means used during the second coating stage is preferably not the one used during the first coating stage but it is possible to use the same conveying means for both coating stages. The powder applied during each coating stage will usually be the same but it is of course possible to apply different powders at each stage; similarly the same thickness of coating will usually be applied at each stage but different thicknesses may be applied, if desired.

If desired still further coating stages may be employed for example to apply powder to sides of the products, if the sides have not already been coated.

Preferably the conveying means comprises a conveyor belt. The conveying means may however comprise an inclined static surface or a vibrated surface along which the cores slide. The friction between the cores and the inclined surface may be reduced by passing air through the inclined surface from the underside.

Converting the powder into a fused film may advantageously comprise converting the powder into the liquid phase after which it returns to the solid phase.

We have found that the conversion of the dry powder into a fused film not only serves to secure the coating to the core but also provides a means by which the distribution of the coating material over the core may be made more even. In some cases the coating material may have such a low viscosity when fused that the coating will distribute itself evenly over a core but in most cases the coating material will be more viscous and the method therefore preferably includes the further mechanical treatment of the coating to even out the depth of the coating over the surface of the core. The evening out step may be carried out by passing the cores under a vibrating plate or a rotating roller, the plate or roller contacting and evening out the coating on the core. Alternatively the evening out step may be carried out by passing the cores under a jet of air, for example an air knife, the curtain of air generated as the air knife evening out the coating on the core; the air may be heated in order to avoid premature solidifying of the coating.

The dry powder coating is converted into a fused film by heating, preferably by infra red radiation, but other forms of electromagnetic radiation may be used. Usually the change in the coating upon heating will simply be a physical change from

a powder to a liquid and then, on cooling, to a continuous solid coating, but there are other possibilities: for example, the powder coating may comprise a polymer which is cured during the treating step, for example by irradiation with energy in the gamma, ultra violet or radio frequency bands, to form a continuous cross-linked polymer coating.

It is preferable to charge the powder to an appropriate electric potential, which may be positive or negative. The powder is preferably charged as it is supplied to the region through which the conveying means passes. The charging may be carried out using a corona charging apparatus; another possibility is to charge the powder triboelectrically. One or more electrodes maintained at a selected potential which would normally be of the same sign as that of the powder (i.e. a positive potential if the powder is positively charged and a negative potential if the powder is negatively charged) are preferably provided above the conveying means in the region to which the powder is supplied. The positioning of the electrodes and the potential(s) at which they are maintained influences the electric field in the region and therefore the path of the powder through the region.

The conveying means is preferably maintained at a potential which is either earth potential or of opposite sign to the potential to which the powder is charged. The conveying means may have an electrically conducting upper surface on which the tablet cores rest. In most cases the cores will be made of an electrically insulating material; they may be treated prior to application of the powder to make them more electrically conducting, for example by moistening the exterior of the core. Such moistening facilitates the maintenance of the exterior of the core at earth potential and thus facilitates the application of the powder to the core.

The method of the invention is not restricted to the use of any particular form of coating material. On the other hand, for good results, the dry powder preferably has the following physical properties:

(1) A particle size in the range of 1 μm to 1000 μm and preferably in the range of 30 μm to 80 μm ; a small particle size enables the powder to be evenly dispersed in the region to which it is supplied and through which the conveyor belt passes.

(2) A relatively high resistivity in the range of $10^6 \Omega\text{m}$ to $10^{24} \Omega\text{m}$ and preferably in the range of $10^9 \Omega\text{m}$ to $10^{14} \Omega\text{m}$; a high resistivity facilitates maintenance of the powder charge but makes it harder to charge the powder.

(3) A viscosity when in the liquid phase of less than 500 Pas and preferably less than 75 Pas; a low viscosity facilitates even spreading of the

coating over the surface of the tablet core.

(4) After conversion to a fused film, a tensile strength of more than 0.5 N/m² and preferably more than 3.5 N/m²; a reasonably strong and tough coating is required in order to protect the tablet during subsequent handling up to the administration of the tablet.

(5) A melting point which lies in the range of 50 °C to 180 °C and preferably 60 °C to 100 °C. With a relatively low melting point less energy is required to convert the powder into the liquid phase and the risk of damage to the tablet core from heating is reduced. The latter point is of special importance when the drug in the tablet core is liable to be damaged if its temperature is increased substantially above room temperature.

Examples of materials which, alone or when blended with other materials, meet some or all of the five preferred properties listed above can be found in: polyamides, polyalkenes, waxes, oils, polyesters, sugar alcohols, sugars, polyox-yethylenes and ethylene vinyl acetate copolymer. Examples of suitable sugar alcohols are: sorbitol and xylitol. Examples of suitable sugars are sucrose and lactose. A polyester having properties especially suitable for the method of the invention is polycaprolactone.

The materials indicated above may be modified by blending other materials with them so as to improve their physical properties to match more closely the properties indicated above. One or more opacifiers, for example titanium dioxide, and/or colourants, for example aluminium lakes or dyes, may also be added to the formulation of the coating material.

The materials listed above fall into two categories: the water soluble materials (polyox-yethylenes, sugars, sugar alcohols) and the poorly soluble or insoluble polymeric materials. If a coating is required to dissolve quickly following administration, then a water soluble material will generally be preferred whereas if a delayed, controlled or modulated release of the drug is required a poorly soluble or insoluble polymeric material is likely to be advantageous.

An especially preferred sugar alcohol is xylitol, while an especially preferred polymeric material is a polyester, such as, for example polycaprolactone. In both cases, however, it may be desirable to add small quantities of other substances to improve the physical properties of the material.

The invention may be used to apply a coating of controlled thickness and may be employed for a pharmaceutical tablet containing a drug that is to be instantaneously released when administered or that is to be the subject of controlled or modulated release, such control or modulation being achieved from the nature of the coating and/or from the

nature of the core. Where the desired form of release is to be achieved by characteristics of the coating, it may be preferred to leave one portion of the product uncoated or coated with a different material. In the case of a tablet having faces at opposite ends connected by a cylindrical side wall, the portion that is uncoated or coated with a different material may be one of the faces of the tablet, a small portion of one of the faces or a side wall of the tablet.

As has already been made clear, the methods described above have the advantage that they can be carried out continuously. They can therefore be employed as part of a continuous process for producing coated cores of pharmaceutical tablets.

The present invention also provides a continuous process for producing coated tablets comprising the steps of:

continuously forming pharmaceutical tablet cores on a rotary press, and

continuously coating the tablet cores by a method as defined above.

The present invention also provides an apparatus for carrying out a method of coating pharmaceutical tablet cores as defined above, the apparatus including:

a conveying means,

means for feeding cores onto the conveying means,

a feed for supplying coating material to a region through which the conveying means passes,

electric charging means for electrically charging the coating material and/or the conveying means and/or the cores such that the potential of the coating material supplied to the region through which the conveying means passes is different from the potential of the cores on the conveying means, whereby the coating material is attracted to the exposed surfaces of the cores to form coatings thereon, characterised in that the coating material is a dry powder and that the apparatus further includes means for melting the dry powder attracted to the cores to convert the powder into fused film coatings secured to the cores.

The apparatus may further include a rotary press, wherein the feeding means is operative to feed the cores from the press onto the conveying means.

The present invention also provides a pharmaceutical tablet when coated by a method as described above.

The invention also provides the use of a dry powder having a melting point which lies in the range 50°C to 180°C in a method as herein described.

The invention additionally provides the use of a dry powder consisting wholly or substantially of one or more of the materials in the group compris-

ing: polyamides, polyalkenes, waxes, oils, polyesters, polyoxyethylenes, sugars, sugar alcohols and ethylene vinyl acetate copolymer in a method as herein described.

A method and apparatus for electrostatic coating of tablet cores will now be described by way of example with reference to the accompanying drawings of which:

Fig. 1 is a schematic side view of an apparatus for coating tablets on one face,

Fig. 2 is a block diagram of a continuous process for manufacturing coated tablets employing the apparatus of Fig. 1, and

Fig. 3 is a side view of a coated tablet.

The apparatus shown in Fig. 1 includes a conveyor belt 1 which is guided around three idler rollers 2 and a drive roller 3 driven by a motor 4 in the direction shown by an arrow in Fig. 1. A booth 5 is provided enclosing most of the upper run of the conveyor belt 1.

Apparatus for feeding tablet cores to the upstream end (the left hand end as seen in Fig. 1) of the conveyor belt 1 outside the booth 5 is provided, but is not shown in the drawing. The form of such apparatus is not part of the present invention. A feed for supplying dry powder to the interior of the booth above the conveyor belt is also provided. In the example of the invention illustrated the feed comprises an electrostatic powder gun 6 employing a single fixed corona electrode 7 mounted at the end of the gun barrel 8 and connected to a voltage supply 9. A mixture of powder and air is fed to the gun barrel from a venturi powder feed 10.

Suspended from the top of the booth is an electrode 11 which is rectangular in plan view and extends across the whole width of the conveyor belt 1 and a portion of its length. The electrode 11 is connected to a voltage supply 12. Immediately below and supporting the conveyor belt 1 in the region below the electrode 11 is another rectangular electrode 18 which is connected to earth. The conveyor belt 1 is made of a laminate of polyvinylchloride and aluminium foil with the aluminium foil forming the outer layers of the belt and the belt is connected to earth.

An infra red heater 13 and a vibrating plate 14 are provided over the downstream end of the conveyor belt.

In use of the apparatus, pharmaceutical tablet cores are fed onto the upstream end of the belt 1 by a feed and pass along the conveyor with one face of the core resting on the belt and the other facing upwards. Dry powder with which the tablet cores are to be coated is sprayed into the booth 5 by the spray gun 6 which charges the powder to a suitable potential (for this example it will be as-

sumed that the powder is charged to a positive potential). Powder sprayed from the gun 6 enters the region between the electrode 11, which is maintained at a positive potential, and the conveyor belt 1 and electrode 18 both of which are earthed. Thus powder is directed downwardly away from the electrode 11 towards the conveyor belt 1 and the electrode 18. A coating of powder is therefore laid over the conveyor belt and the tablet cores on the conveyor belt.

The tablet cores are then passed under the infra red heater 13 which heats the coating of powder on the tablets sufficiently to cause the coating to melt and form a film coating over the upper side of the tablet core. As the tablets are carried beyond the heater 13 they are contacted by the vibrating plate 14 which evens out the coating. Thereafter, the film coating solidifies.

In order to provide a coating on the other side of the tablet core (if one is desired), the tablets are laid the other way up on a further conveyor arrangement similar to that shown in Fig. 1 and the process described above with respect to Fig. 1 is repeated. Apparatus for transferring tablets from one conveyor to another and for turning them over in the course of the transfer is already known (see for example Figs. 2 and 3 of GB 1 075 404).

Referring now to Fig. 2, it will be seen that with the apparatus and method just described a continuous production of coated tablets can be provided. Tablet cores produced for example from a high speed rotary press are fed directly to the apparatus of Fig. 1 where their upper faces are coated with electrically charged dry powder. The dry powder coating is then melted by heating, the partially coated tablets allowed to cool and fed to another apparatus of the kind shown in Fig. 1 but with their uncoated faces now uppermost. Those uncoated faces are coated with electrically charged dry powder, the dry powder coating is melted by heating and the coated tablet allowed to cool and then fed to appropriate packaging machinery. Such a process can operate continuously.

Fig. 3 shows a tablet having an upper face 15, a lower face 16, and a cylindrical side wall 17. In the first coating stage, one of the faces, say the face 15, is coated fully and the side wall 17 receives some powder coating but not a full coating. In the second coating stage the other face 16 is coated fully and the remainder of the coating to the side walls 17 is applied.

Claims

1. A method of coating cores of pharmaceutical tablets with a coating material, the method including the following steps:
feeding the cores onto a conveying

means;

supplying coating material to a region through which the cores are to be conveyed on the conveying means; and

conveying the cores on the conveying means through the region with the cores maintained at a different electric potential from the coating material, whereby the coating material is attracted to the exposed surfaces of the cores to form coatings thereon,

characterised in that the coating material is a dry powder and that after the dry powder is attracted to the exposed surfaces of the cores to form coatings thereon the dry powder is melted to convert the powder into fused film coatings secured to the cores.

2. A method according to claim 1, in which the method is carried out as a continuous process.

3. A method according to claim 1 or 2, including the following further subsequent steps:

feeding the tablet cores onto a conveying means with the fused film coatings of the cores in contact with the conveying means and with that surface of the core that was in contact with the conveying means during the above-mentioned conveying step exposed;

supplying the dry powder with which the cores are to be coated to a region through which the conveying means passes;

conveying the cores on the conveying means through the region with the conveying means and/or the cores maintained at a different electric potential from the dry powder whereby the dry powder is attracted to the exposed surfaces of the cores, and

melting the dry powder coatings to convert the newly applied powder into fused film coatings secured to the cores.

4. A method according to claim 3, in which the conveying means used during the second coating stage is not the one used during the first coating stage.

5. A method according to any preceding claim, in which the conveying means comprises a conveyor belt.

6. A method according to any preceding claim including a further mechanical treatment of the coating to even out the depth of the coating over the surface of the core.

7. A method according to claim 6, in which the evening out step is carried out by passing the cores under a vibrating plate or a rotating

- roller, the plate or roller contacting and evening out the coating on the core.
8. A method according to claim 6, in which the evening out step is carried out by passing the cores under a jet of air.
 9. A method according to any preceding claim, in which the powder is electrically charged.
 10. A method according to claim 9, in which the powder is charged as it is supplied to the region through which the conveying means passes.
 11. A method according to claim 9 or 10, in which the charging is carried out using a corona charging apparatus.
 12. A method according to any preceding claim, in which one or more electrodes maintained at a selected potential are provided above the conveying means in the region to which the powder is supplied.
 13. A method according to any preceding claim, in which the powder has a particle size in the range of $1\text{ }\mu\text{m}$ to $1000\text{ }\mu\text{m}$.
 14. A method according to any preceding claim, in which the powder has a relatively high resistivity in the range of 10^6 to $10^{24}\text{ }\Omega\text{m}$.
 15. A method according to any preceding claim, in which the powder has a viscosity when in the liquid phase of less than 500 Pas .
 16. A method according to any preceding claim, in which the powder has, after returning to the solid phase, a tensile strength of more than 0.5 N/m^2 .
 17. A method according to any preceding claim, in which the powder has a melting point which lies in the range of 50°C to 180°C .
 18. A method according to claim 17, in which the powder has a melting point in the range of 60°C to 100°C .
 19. A method according to any preceding claim, in which the dry powder consists wholly or substantially of one or more of the materials in the group comprising: polyamides, polyalkenes, waxes, oils, polyesters, polyoxyethylenes, sugars, sugar alcohols and ethylene vinyl acetate copolymer.
 20. A method according to claim 19, in which the dry powder consists wholly or substantially of xylitol.
 21. A method according to any preceding claim in which the dry powder consists wholly or substantially of polycaprolactone.
 22. A method according to any preceding claim, in which the tablet cores are treated prior to application of the powder to make them more electrically conducting.
 23. A method according to claim 22, in which the treatment comprises moistening the exterior of the tablet cores.
 24. A continuous process for producing coated tablets comprising the steps of:
 - continuously forming pharmaceutical tablet cores on a rotary press, and
 - continuously coating the tablet cores by a method according to any preceding claim.
 25. An apparatus for carrying out a method according to any of claims 1 to 23, the apparatus including:
 - a conveying means,
 - means for feeding the cores onto the conveying means,
 - a feed for supplying coating material to a region through which the conveying means passes,
 - electric charging means for electrically charging the coating material and/or the conveying means and/or the cores such that the potential of the coating material supplied to the region through which the conveying means passes is different from the potential of the cores on the conveying means, whereby the coating material is attracted to the exposed surfaces of the cores to form coatings thereon, characterised in that the coating material is a dry powder and that the apparatus further includes means for melting the dry powder attracted to the cores to convert the powder into fused film coatings secured to the cores.
 26. An apparatus according to claim 25, the apparatus further including a rotary press, wherein the feeding means is operative to feed the cores from the press onto the conveying means.
 27. An apparatus according to claim 25 or 26, wherein the conveying means comprises an inclined static surface.

28. A pharmaceutical tablet when coated by a method according to any one of claims 1 to 23.
29. A tablet when produced by a method according to claim 24.
30. The use of a dry powder having a melting point which lies in the range of 50 °C to 180 °C in a method as claimed in any of claims 1 to 23.
31. The use of a dry powder consisting wholly or substantially of one or more of the materials in the group comprising: polyamides, polyalkenes, waxes, oils, polyesters, polyoxyethylenes, sugars, sugar alcohols and ethylene vinyl acetate copolymer in a method as claimed in any of claims 1 to 23.
32. The use according to claim 31 of a dry powder consisting wholly or substantially of ethylene vinyl acetate copolymer.
33. The use according to claim 31 of a dry powder consisting wholly or substantially of a sugar alcohol selected from sorbitol and xylitol.

Patentansprüche

1. Verfahren zum Überziehen der Kerne von pharmazeutischen Tabletten mit einem Überzugsmaterial, wobei das Verfahren die folgenden Stufen umfaßt:
Zuführen der Kerne auf ein Beförderungsmittel;
Anliefern von Überzugsmaterial zu einer Zone, durch die hindurch die Kerne auf dem Beförderungsmittel befördert werden sollen; und
Befördern der Kerne auf dem Beförderungsmittel durch die Zone, wobei die Kerne bei einem von dem Überzugsmaterial unterschiedlichen elektrischen Potential gehalten werden, wodurch das Überzugsmaterial von den exponierten Oberflächen der Kerne unter Bildung von Überzügen darauf angezogen wird, dadurch gekennzeichnet, daß das Überzugsmaterial ein trockenes Pulver ist und daß, nachdem das trockene Pulver von den exponierten Oberflächen der Kerne unter Bildung von Überzügen darauf angezogen worden ist, das trockene Pulver geschmolzen wird, um das Pulver zu verschmolzenen Filmüberzügen, die auf den Kernen befestigt sind, umzuwandeln.
2. Verfahren nach Anspruch 1, bei dem das Verfahren als kontinuierliches Verfahren durchgeführt wird.
3. Verfahren nach Anspruch 1 oder 2 einschließlich der folgenden zusätzlichen anschließenden Stufen:
Zuführen der Tablettenkerne auf ein Beförderungsmittel, wobei die verschmolzenen Filmüberzüge der Kerne in Kontakt sind mit dem Beförderungsmittel und wobei diejenige Oberfläche des Kerns exponiert ist, die mit dem Beförderungsmittel während der oben genannten Beförderungsstufe in Kontakt war;
Zuführen des trockenen Pulvers, mit dem die Kerne überzogen werden sollen, in eine Zone, durch die das Beförderungsmittel hindurchläuft;
Befördern der Kerne auf dem Beförderungsmittel durch die Zone, wobei das Beförderungsmittel und/oder die Kerne bei einem von dem trockenen Pulver unterschiedlichen elektrischen Potential gehalten werden, wodurch das trockene Pulver von den exponierten Oberflächen der Kerne angezogen wird; und
Schmelzen der trockenen Pulverüberzüge, um das neu aufgetragene Pulver zu verschmolzenen Filmüberzügen umzuwandeln, die auf den Kernen befestigt sind.
4. Verfahren nach Anspruch 3, bei dem das Beförderungsmittel, das während der zweiten Überzugsstufe verwendet wird, nicht dasjenige ist, das während der ersten Überzugsstufe verwendet wird.
5. Verfahren nach einem vorhergehenden Anspruch, bei dem das Beförderungsmittel ein Förderband umfaßt.
6. Verfahren nach einem vorhergehenden Anspruch einschließlich einer weiteren mechanischen Behandlung des Überzugs, um die Dicke des Überzugs über der Kernoberfläche zu nivellieren.
7. Verfahren nach Anspruch 6, bei dem die Nivellierungsstufe durchgeführt wird, indem die Kerne unter einer vibrierenden Platte oder einer rotierenden Walze hindurchgeführt werden, wobei die Platte oder die Walze den Überzug auf dem Kern berührt und nivelliert.
8. Verfahren nach Anspruch 6, bei dem die Nivellierungsstufe durchgeführt wird, indem die Kerne unter einem Luftstrahl hindurchgeführt werden.
9. Verfahren nach einem vorhergehenden Anspruch, bei dem das Pulver elektrisch geladen wird.

10. Verfahren nach Anspruch 9, bei dem das Pulver geladen wird, wenn es der Zone zugeführt wird, durch die das Beförderungsmittel hindurchläuft.
11. Verfahren nach Anspruch 9 oder 10, bei dem das Laden unter Anwendung eines Corona-Ladegerätes durchgeführt wird.
12. Verfahren nach einem vorhergehenden Anspruch, bei dem eine oder mehrere Elektroden, die bei einem gewählten Potential gehalten werden, über dem Beförderungsmittel in der Zone bereitgestellt werden, der das Pulver zugeführt wird.
13. Verfahren nach einem vorhergehenden Anspruch, bei dem das Pulver eine Teilchengröße im Bereich von 1 μm bis 1000 μm besitzt.
14. Verfahren nach einem vorhergehenden Anspruch, bei dem das Pulver einen relativ hohen spezifischen Widerstand im Bereich von 10^6 bis 10^{24} Ωm besitzt.
15. Verfahren nach einem vorhergehenden Anspruch, bei dem das Pulver eine Viskosität von weniger als 500 Pas besitzt, wenn es sich in der flüssigen Phase befindet.
16. Verfahren nach einem vorhergehenden Anspruch, bei dem das Pulver nach Rückkehr in die feste Phase eine Zugfestigkeit von mehr als 0,5 N/m² besitzt.
17. Verfahren nach einem vorhergehenden Anspruch, bei dem das Pulver einen Schmelzpunkt besitzt, der im Bereich von 50 °C bis 180 °C liegt.
18. Verfahren nach Anspruch 17, bei dem das Pulver einen Schmelzpunkt im Bereich von 60 °C bis 100 °C besitzt.
19. Verfahren nach einem vorhergehenden Anspruch, bei dem das trockene Pulver vollständig oder im wesentlichen aus einem oder mehreren der Materialien aus der Gruppe besteht, die umfaßt:
Polyamide, Polyalkene, Wachse, Öle, Polyester, Polyoxyethylene, Zucker, Zuckeralkohole und Ethylvinylacetat-Copolymer.
20. Verfahren nach Anspruch 19, bei dem das trockene Pulver vollständig oder im wesentlichen aus Xylit besteht.
21. Verfahren nach einem vorhergehenden Anspruch, bei dem das trockene Pulver vollständig oder im wesentlichen aus Polycaprolacton besteht.
22. Verfahren nach einem vorhergehenden Anspruch, bei dem die Tablettenkerne vor dem Auftragen des Pulvers behandelt werden, um sie elektrisch leitender zu machen.
23. Verfahren nach Anspruch 22, bei dem die Behandlung das Befeuchten des Äußeren der Tablettenkerne umfaßt.
24. Kontinuierliches Verfahren zur Herstellung überzogener Tabletten, welches die Stufen umfaßt:
kontinuierliches Bilden von pharmazeutischen Tablettenkernen auf einer Rotationspresse, und
kontinuierliches Überziehen der Tablettenkerne durch ein Verfahren gemäß einem vorhergehenden Anspruch.
25. Gerät zur Durchführung eines Verfahrens nach einem der Ansprüche 1 bis 23, wobei das Gerät einschließt:
ein Beförderungsmittel,
Mittel zum Zuführen der Kerne auf das Beförderungsmittel,
einen Vorschub zum Zuführen von Überzugsmaterial in einer Zone, durch die das Beförderungsmittel hindurchläuft,
elektrische Ladungsmittel zum elektrischen Laden des Überzugsmaterials und/oder des Beförderungsmaterials und/oder der Kerne, so daß das Potential des Überzugsmaterials, das der Zone zugeführt worden ist, durch die das Beförderungsmittel hindurchläuft, sich von dem Potential der Kerne auf dem Beförderungsmittel unterscheidet; wodurch das Überzugsmaterial von den exponierten Oberflächen der Kerne unter Bildung von Überzügen darauf angezogen wird,
dadurch gekennzeichnet, daß das Überzugsmaterial ein trockenes Pulver ist und daß das Gerät außerdem Mittel zum Schmelzen des trockenen Pulvers einschließt, das von den Kernen angezogen worden ist, um das Pulver zu verschmolzenen Filmüberzügen umzuwandeln, die an den Kernen befestigt sind.
26. Gerät nach Anspruch 25, wobei das Gerät außerdem eine Rotationspresse einschließt, in der das Vorschubmittel betrieben wird, um die Kerne von der Presse auf das Beförderungsmittel zu befördern.

27. Gerät nach Anspruch 25 oder 26, worin das Beförderungsmittel eine geneigte statische Oberfläche einschließt.

28. Pharmazeutische Tablette nach dem Überziehen durch ein Verfahren gemäß einem der Ansprüche 1 bis 23.

29. Tablette nach der Herstellung durch ein Verfahren nach Anspruch 24.

30. Verwendung eines trockenen Pulvers mit einem Schmelzpunkt, der im Bereich von 50 °C bis 180 °C liegt, bei einem Verfahren nach einem der Ansprüche 1 bis 23.

31. Verwendung eines trockenen Pulvers, bestehend vollständig oder im wesentlichen aus einem oder mehreren der Materialien in der Gruppe, umfassend: Polyamide, Polyalkene, Wachse, Öle, Polyester, Polyoxyethylene, Zucker, Zuckeralkohole und Ethylenvinylacetat-Copolymer bei einem Verfahren nach einem der Ansprüche 1 bis 23.

32. Verwendung nach Anspruch 31 eines trockenen Pulvers, bestehend vollständig oder im wesentlichen aus Ethylenvinylacetat-Copolymer.

33. Verwendung nach Anspruch 31 eines trockenen Pulvers, bestehend vollständig oder im wesentlichen aus einem Zuckeralkohol, ausgewählt aus Sorbit und Xylit.

Revendications

1. Méthode d'enrobage de noyaux de comprimés pharmaceutiques d'une matière d'enrobage, méthode comprenant les étapes suivantes :

alimentation en noyaux sur un moyen de convoyage :

fourniture de la matière d'enrobage à une zone à travers laquelle les noyaux doivent être convoyés sur le moyen de convoyage ; et

convoyage des noyaux sur le moyen de convoyage à travers ladite zone, les noyaux étant maintenus à un potentiel électrique différent de celui de la matière d'enrobage, suite à quoi la matière d'enrobage est attirée vers les surfaces exposées des noyaux pour former des enrobages sur celles-ci,

caractérisée en ce que la matière d'enrobage est une poudre sèche et que, ensuite, la poudre sèche est attirée vers les surfaces exposées des noyaux pour former des enrobages sur celles-ci, la poudre sèche est fondue pour convertir la poudre en pellicules d'enro-

bage fondues attachées aux noyaux.

2. Méthode selon la revendication 1, où la méthode est mise en oeuvre sous forme d'un procédé en continu.

3. Méthode selon les revendications 1 ou 2, comprenant les étapes suivantes :

alimentation en noyaux de comprimés sur un moyen de convoyage avec les pellicules d'enrobage de noyaux fondues étant en contact avec le moyen de convoyage et avec celle des surfaces du noyau qui était exposée, en contact avec le moyen de convoyage, pendant l'étape de convoyage ci-dessus ;

fourniture de la poudre sèche, de laquelle on doit revêtir les noyaux, à une zone à travers laquelle passe le moyen de convoyage ;

convoyage des noyaux sur le moyen de convoyage à travers la zone avec le moyen de convoyage et/ou les noyaux maintenus à un potentiel électrique différent de celui de la poudre sèche, suite à quoi la poudre sèche est attirée vers les surfaces exposées des noyaux, et

fusion des enrobages de poudre sèche pour transformer la poudre nouvellement appliquée en pellicules d'enrobage fondues attachées aux noyaux.

4. Méthode selon la revendication 3, où le moyen de convoyage utilisé pendant la deuxième étape d'enrobage n'est pas celui utilisé dans la première étape d'enrobage.

5. Méthode selon l'une quelconque des revendications précédentes, où le moyen de convoyage comprend une bande transporteuse.

6. Méthode selon l'une quelconque des revendications précédentes, comprenant un traitement mécanique ultérieur de l'enrobage pour égaliser les irrégularités de l'enrobage sur la surface du noyau.

7. Méthode selon la revendication 6, où l'étape d'égalisation est mise en oeuvre en faisant passer les noyaux sous une table vibrante ou un cylindre rotatif, la table ou le cylindre étant en contact avec l'enrobage et effectuant l'égalisation de l'enrobage sur le noyau.

8. Méthode selon la revendication 6, où l'étape d'égalisation est mise en oeuvre en faisant passer les noyaux sous un jet d'air.

9. Méthode selon l'une quelconque des revendications précédentes, où la poudre est chargée

par énergie électrique.

10. Méthode selon la revendication 9, où on charge la poudre au fur et à mesure de la fourniture de celle-ci à la zone à travers laquelle passe le moyen de convoyage. 5
11. Méthode selon la revendication 9 ou 10, où on met en oeuvre le chargement en utilisant un appareil de chargement corona. 10
12. Méthode selon l'une quelconque des revendications précédentes, où une ou plusieurs électrodes à un potentiel choisi sont maintenues au-dessus du moyen de convoyage dans la zone à laquelle on fournit la poudre. 15
13. Méthode selon l'une quelconque des revendications précédentes, où la poudre a une taille de particules dans l'intervalle de 1 μm à 1000 μm . 20
14. Méthode selon l'une quelconque des revendications précédentes, dans laquelle la poudre a une résistivité relativement élevée dans l'intervalle de 10^6 à 10^{24} Ωm . 25
15. Méthode selon l'une quelconque des revendications précédentes, où la poudre a une viscosité en phase liquide inférieure à 500 Pas. 30
16. Méthode selon l'une quelconque des revendications précédentes où la poudre, après avoir passé à nouveau en phase solide, a une résistance à la traction supérieure à 0,5 N/m². 35
17. Méthode selon l'une quelconque des revendications précédentes, où la poudre a un point de fusion dans l'intervalle de 50 °C à 180 °C. 40
18. Méthode selon la revendication 17, où la poudre a un point de fusion dans l'intervalle de 60 °C à 100 °C. 45
19. Méthode selon l'une quelconque des revendications précédentes, où la poudre sèche est composée entièrement ou substantiellement d'une ou plusieurs matières prises dans le groupe comprenant : les polyamides, les polyalkylènes, les cires, les huiles, les polyesters, les oxydes de polyéthylène, les sucres, les alcools de sucre et le copolymère de l'éthylène-acétate de vinyle. 50
20. Méthode selon la revendication 19, où la poudre sèche est composée entièrement ou substantiellement de xylitol. 55
21. Méthode selon l'une quelconque des revendications précédentes, où la poudre sèche est composée entièrement ou substantiellement de polycaprolactone.
22. Méthode selon l'une quelconque des revendications, où on traite les noyaux de comprimés avant application de la poudre pour augmenter leur conductivité électrique.
23. Méthode selon la revendication 22, où le traitement comprend l'humidification de l'extérieur des noyaux de comprimés.
24. Procédé en continu pour préparer des comprimés enrobés comprenant les étapes de :
moulage en continu des noyaux de comprimés pharmaceutiques dans une presse rotative, et
enrobage en continu des noyaux de comprimés à l'aide d'une méthode selon l'une quelconque des revendications précédentes.
25. Appareil pour la mise en oeuvre d'une méthode selon l'une quelconque des revendications 1 à 23, appareil comprenant :
un moyen de convoyage,
moyen d'alimentation des noyaux sur le moyen de convoyage,
une alimentation pour fournir la matière d'enrobage dans une zone à travers laquelle passe le moyen de convoyage,
moyen de chargement électrique pour charger d'électricité la matière d'enrobage et/ou le moyen de convoyage et/ou les noyaux de sorte que le potentiel de la matière d'enrobage fournie à la zone traversée par le moyen de convoyage soit différent du potentiel des noyaux sur le moyen de convoyage, suite à quoi la matière d'enrobage est attirée vers les surfaces exposées des noyaux pour former un enrobage sur celles-ci,
caractérisée en ce que la matière d'enrobage est une poudre sèche et que l'appareil comprend de plus des moyens pour fondre la poudre sèche attirée vers les noyaux en vue de transformer la poudre en pellicule d'enrobage fondue attachée aux noyaux.
26. Appareil selon la revendication 25, l'appareil comprend de plus une presse rotative, dans laquelle le moyen d'alimentation est opérationnel pour transférer les noyaux de la presse sur le moyen de convoyage.
27. Appareil selon la revendication 25 ou 26, où le moyen de convoyage comprend une surface statique inclinée.

28. Comprimé pharmaceutique lorsqu'il est enrobé à l'aide d'une méthode selon l'une quelconque des revendications 1 à 23.
29. Comprimé lorsqu'il est préparé à l'aide d'une méthode de la revendication 24. 5
30. Utilisation d'une poudre sèche ayant un point de fusion dans l'intervalle de 50 °C à 180 °C dans une méthode selon l'une quelconque des revendications 1 à 23. 10
31. Utilisation d'une poudre sèche composée entièrement ou substantiellement d'une ou plusieurs matières prises dans le groupe comprenant : les polyamides, les polyalkylènes, les cires, les huiles, les polyesters, les oxydes de polyéthylène, les sucres, les alcools de sucre et le copolymère de l'éthylène-acétate de vinyle dans une méthode selon l'une quelconque des revendication 1 à 23. 15 20
32. Utilisation selon la revendication 31, d'une poudre sèche composée entièrement ou substantiellement de copolymère de l'éthylène-acétate de vinyle. 25
33. Utilisation selon la revendication 31, d'une poudre sèche composée entièrement ou substantiellement d'un alcool de sucre choisi parmi le sorbitol et le xylitol. 30

35

40

45

50

55

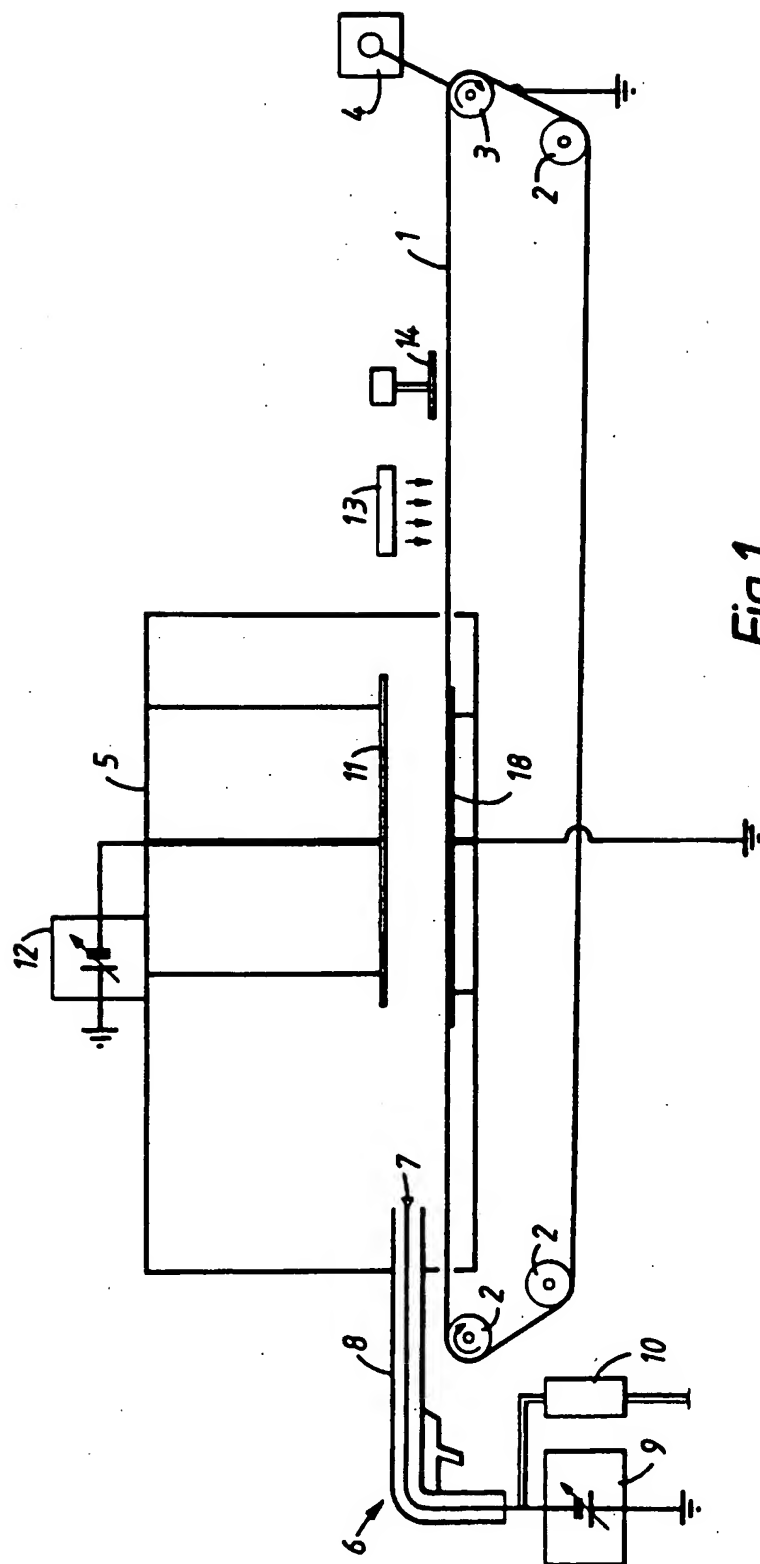


Fig. 1.

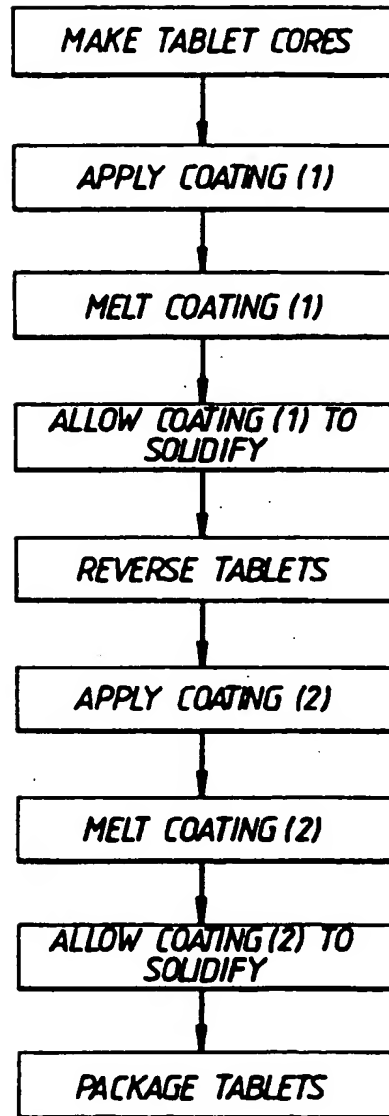


Fig.2.

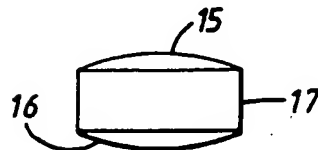


Fig.3.

**This Page is Inserted by IFW Indexing and Scanning
Operations and is not part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☒ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☒ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☒ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.